NEW PHARMACOLOGICAL CHARACTERISTICS OF DRY EXTRACT OF ACHILLEA MILLEFOLIUM L. MEDICINAL PLANT GROWING IN UZBEKISTAN

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Abstract: *In separate experiments, he studied the effects of the studied dry extracts on the body and individual internal organs when they are loaded into the body during long-term exposure. As a result of the conducted analysis, it was found that there are no drug-related changes in the studied building elements, the time of coagulation of the mine, the activity of the cardiovascular system, and the mathematical levels of the weight category. In the structure of these organizations studying the histostructure of the internal affairs bodies, the studied construction defended the variables associated with the extract.*

Therefore, the studied dry extract did not cause pathological changes in the animal organism at the studied doses.

Key words: *Achillea Mellifolium L.; Herba Meliloti L, dry extract, carbidopa, blood, coagulation system, medicinal plants, hemopoiesis.*

INTRODUCTION

Currently, in the field of medicine, the selection of a local drug with high therapeutic activity, relatively few side effects and low cost in pharmacotherapy is a very important issue [1]. It is known that the most common diseases in the elderly include atherosclerosis, arterial hypertension and other cardiovascular diseases. The main clinical signs associated with these diseases are blood coagulation disorders, increased blood pressure, diuresis and related pathological processes [2].

In order to find a solution to this problem, the dry extract of Achillea Mellifolium (Achillea Mellifolium L.) medicinal plant in folk medicine was used by the staff of the Tashkent Pharmaceutical Institute as a hypotensive and diuretic local medicine. the drug has a mild hypotensive and diuretic effect, and it slightly accelerates the process of blood clotting in our elderly. This has limited the possibility of using the common anti-aging drug in clinics on a large scale. Because the blood coagulation process is increased compared to the norm in diseases such as atherosclerosis, arterial hypertension, thrombosis, rheumatism, arthritis and heart failure in our elderly people [3].

Therefore, the search for local, low-toxic plant extracts free from the side effects of reducing blood coagulation in the treatment of the above-mentioned cardiovascular diseases and their application to medicine is one of the important issues of modern medicine.

According to the information provided by the World Health Organization, about 60% of the population of the planet are using drugs used in folk medicine. In some countries, the science of folk medicine is included in the medical system. In some countries, the use of folk medicine - traditional medicine is more than the use of modern medicine methods. For example, according to K. G. Gurevich, the use of traditional medicine is 80 percent in Africa and 65 percent in India. Even in developed countries there is a great interest in traditional medicine methods. In particular, recourse to traditional medicine methods is 48% in Australia, 70% in Canada, 75% in France, 40% in Belgium, 42% in the USA [4]. In 1999, an epidemiological study conducted in the United States showed that 29% of middle-aged Americans use traditional medicine, and 10% use herbal remedies [5].

It is known that in the past, the science of medicine, like other sciences, was very widely developed in the territory of Central Asia. It is self-evident that the reason for this is that not only ordinary people, scholars, but also state and religious figures have made a great contribution to the development of this science. In fact, our prophet Muhammad, may God bless him and grant him peace, devoted some of his hadiths to the study of medicine. On the basis of these hadiths, treatises entitled "Prophetic Medicine" were created [6]. In conclusion, it can be said that where the science of medicine develops, the development of other sciences is also noted there. That's why our thinkers, great scientists and brilliant doctors who lived and worked in Central Asia laid the foundation for the ancient science of medicine. Our encyclopedic scientists, Abu Bakr ar Razi, Abu Nasir ibn Iraq, Abu Raikhan Beruni, Abu Ali ibn Sina and others, who have written a pen in the field of medicine and are a salve for the pain of our hardworking people, have made a great contribution to world science and medicine.

The above-mentioned encyclopedic scientists treated the pains of our people and patients mainly with drugs created and developed on the basis of local raw materials, medicinal plants, minerals and founded traditional medicine.

The purpose of the study.

It consists in studying the effects of a new plant collection (Herba Meliloti L.) affecting the blood coagulation process, as well as its pharmacology.

Research methods. Experimental pharmacological, hematological, immunological, preclinical toxicological and mathematical methods were used.

Results and its discussion. While studying the pharmacological properties of tinctures and dry extracts of common sedum and saffron (1:1 ratio), we focused on studying their effects on urinary excretion, blood pressure, and blood clotting time. Experiments were conducted on laboratory mice and rats kept on a normal diet in vivarium conditions.

The results obtained from the experiments were made into a mathematical calculation - a book using the Student's levels by the method of microvariation statistics. It was embodied by Z. Roth, M.L. The Litchfield [113] and Litchfield and Wilcoxon [114] methods cited in Belenky [25] were also used.

Acute toxicity of galenic preparations of studied plants was studied in 36 laboratory mice weighing 17-24 g. The studied preparations (infusion, dry extract) were administered orally using a special metal probe.

The effects of common oleander and kashgarbeda tincture and their 1:1 combination of dry extracts on arterial blood pressure and respiration were studied in 4 rabbits weighing 2.3–3.5 kg using an acute method. For this, experimental animals were anesthetized by intraperitoneal injection of 35-45 mg/kg of 1% ethaminal-sodium solution. Then, under aseptic conditions, the carotid artery, trachea, and leg or ear veins were opened, and the carotid artery was connected to a mercury Ludwig monometer, and the trachea was connected to the Marea capsule through a special device.

Arterial blood pressure was recorded on kymograph tape through a mercury monometer connected to the carotid artery in the neck by polyethylene tubes throughout the experiment. To prevent blood clotting, polyethylene tubes were filled with 5% sodium citrate solution, and the tip of a special cannula injected into a blood vessel was filled with 0.1-0.2 ml of heparin solution. At the same time as arterial blood pressure, respiration was recorded using a Marea capsule connected to the animal's trachea.

The tinctures and dry extracts under study were injected into the stomach at the rate of 10, 25 and 50 ml/kg using special catheters previously lowered into the stomach through the esophagus.

In part of the experiments carried out by this acute method, the effect of the studied tincture and dry extracts on some systems of vegetative innervation was studied.

Experiments were performed on small intestine pieces isolated from 10 laboratory rats weighing 140-165 g, anesthetized with 1% ethaminal-sodium solution.

The effect of the studied drugs on peripheral cholinergic systems was concluded based on the change of depressor reactions in arterial blood pressure caused by acetylcholine (0.5-1 ml 0.001% acetylcholine chloride) solution administered intravenously in doses of 0.5-1 μg/kg. The effect of the drugs on the peripheral adrenoreactive systems was assessed by comparing the hypertensive reactions caused by the changes in arterial blood pressure by intravenous injection of 0.01% adrenaline hydrochloride solution in the amount of 10 μg/kg before and after the drug was administered. Also, before and after administration of the drugs, 0.01% histamine administered intravenously with a dose of 0.5–1 μg/kg was released to the surface, depending on the change of depressor reactions in arterial blood pressure, conclusions were drawn on the effect of the drugs on the histaminergic system of the body.

The effect of ordinary bojmodarand and kashqarbed drugs on cardiac bioelectric activity was studied in 4 laboratory rabbits weighing 2.3–3.1 kg of both sexes. Before the experiment, animals were anesthetized by injecting 40-45 mg/kg of 1% ethaminal sodium intraperitoneally, and the electrocardiogram (ECG) of the animals was recorded using a single-channel EKPSCh-4 electrocardiograph using the II- standard method. In this case, the voltage of the electrocardiograph was equal to 1 mV = 1.5 cm and the film speed was equal to 50 mm/sec. The studied infusions and dry extracts were administered orally using a special probe in doses of 10, 25 and 50 ml/kg. ECG was recorded before drug administration and at 15, 30, 45, 60, and 120 minutes of the experiment, and R-R, P-Q, Q-T, and QRS teeth were

calculated as percentages. The results obtained in the animals of the control group were taken as 100% and compared with the results obtained in the experimental group.

Interaction of preparations obtained from studied plants with hypnotics and narcotics Voronina T.A., Nerobkova L.N. and M.M.Nikolaev (partially modified method was studied. Sleep time was determined in mice in the control group by intraperitoneal injection of 70 mg/kg of hexenal or 300 mg/kg of chloral hydrate. Animals in the experimental group were drugged 45 minutes before drug administration, study drugs were given orally in different doses.

In separate experiments, the effect of dry extracts of the studied plants on electrolyte metabolism was studied in 32 rats weighing 155-183 g. Rats were divided into 4 groups of 8, and the concentration of Na and K ions in their blood serum and urine was determined. The animals in the experimental group were orally administered the study drugs at a dose of 50-250 mg/kg, while the animals in the control group were administered the corresponding distilled water.

The amount of Na and K ions in the blood serum and urine of each animal was measured separately, and the amount of electrolytes in these animals before and after drug administration was determined. The obtained results were compared with the results obtained in the control group. The amount of Na and K ions in the blood and urine of animals was measured.

The effect of the studied drugs on the blood clotting time and the amount of blood released was quoted by N.Ibragimov in his work I.E. Akopov and I.I. 18 laboratory white rats weighing 145–163 g were studied according to the Ibragimov method. 40–45 minutes after administration of the studied preparations or distilled water to the animals of the control and experimental groups, we placed the rats in special chambers adapted to the study of metabolism and clipped them 0.5–1.0 cm from the tip of the tail. To determine the amount of bleeding and how long it took to bleed from the cut, the bleeding was evenly blotted onto pre-dried and weighed filter papers (until the bleeding stopped), then the filter paper was re-dried in a thermostat and weighed (in mg). . Bleeding time was measured with a stopwatch from the time the rats' tails were clipped until the bleeding stopped (in minutes), and the amount of blood released was determined by the weight of the filter paper (in mg). Results obtained from control rats and drug-treated rats were compared.

In separate experiments, the effect of the dry extract of common oleander and the dry extract of the two studied plants on blood-vascular hemostasis, that is, on the amount of platelets and their functional activity, was studied. The amount of platelets, adhesion, spontaneous aggregation was determined by the test tube method, and blood clot retraction was determined by the biochemical method. The method of thromboelastography was used to obtain information about the general process of blood coagulation.

The experiment was conducted in a four-channel thromboelastograph, and the value of the information in the obtained thromboelastogram was evaluated by the following indicators:

R is the reaction time indicating phase I and II of the blood coagulation process;

K – time of formation of coagulated blood;

R/K - used prothrombin constant;

R+K - nonspecific coagulation constant, or total blood clotting time;

MA - maximum amplitude indicating the amount of platelets and their functional activity;

E - coefficient of elasticity of coagulated blood;

ITP - thrombohemorrhagic potential;

Ci – hypercoagulation index.

The studied drugs were injected orally at the rate of 50, 100 mg/kg to experimental rabbits 1 day before and 45-60 minutes before the start of the experiment, and blood was taken before the administration of the drug for analysis and at 30, 60 and 120 minutes of the experiment and on the 2nd day of the experiment. The obtained results were compared. In the study of the chronic toxicity of the drug, special importance was attached to the study of the composition of peripheral blood and the histomorphological structure of internal organs. The experiments were conducted based on the requirements of the Pharmacological Committee of the UzR SSV. On the 30th day of the experiment, some of the animals were killed by decapitation, and small pieces of internal vital organs were taken and fixed in 12% formalin solution. Then 5-7 μm sections were prepared from them and stained with hematoxine-eosin dye and examined by histomorphologists [7,8,9,10,11,12,13,14,15,16,17,18].

The results obtained in the control and experimental groups were compared. Mathematical calculations of the results obtained during all experiments were carried out with an accuracy of R< 0.05.

The effect of the dry extract of the whole plant on blood thromboelastogram indicators (M±m; n=6)

TEG indicators	Normally	Time after administration of the drug, in minutes			
		30′	60′	120′	After 1 day
R, мм	56±4.6	34±2.0*	32±2.1*	38±2.*	66±5.0
K, мм	29±2.0	17±1.4*	14±1.0*	22±2.0*	30±2.0
R+K, мм	85±6.2	51±2.0*	46±4.1*	60±5.0*	96±8.0
R/K	1.9±0.2	2.0±0.1	2.3±0.2	1.7±0.2	2.2±0.2
MA, мм	70±3.8	77±3.4	78±3.0	70±3.3	66±3.3
t, мм	114±12	120±10	110±10	102±10	110±10
S, мм	143±13	135±12	120±12	130±12	140±12
T, мм	200±16	168±15	152±14	167±15	210±18
Ci.	0.82±0.1	1.6±0.1*	1.7±0.12*	1.2±0.1	0.64±0.05*
E.	223±10	241±22	355±24*	233±20	194±20*
ITP	1.6±0.2	1.8±0.2	2.9±0.2*	1.8±0.2	1.4±0.1

Note: *R< 0.05 relative to the norm

The non-specific coagulation constant (R+K) decreased with mathematical precision at the 30th and 120th minutes of the experiment and returned to normal on the 2nd day of the

experiment and became 96±8.0 mm instead of the normal 85±6.2 mm. Similar results were noted in the hypercoagulation index (Ci).

Also, maximum amplitude (MA) and blood elasticity (E) increased by 11% and 59%, respectively, compared to the norm in the 60th minute of the experiment, and significantly decreased on the 2nd day of the experiment. As can be seen from this table, the thrombohemorrhagic potential (ITP) also increased in the 60th minute of the experiment (by 81%). Based on the obtained results, it can be said that when the dry extract obtained from the 1:1 ratio of both plants was administered to the animals, the hemostatic effect typical of the dry extract of common oleander was reduced with mathematical precision on the 1st day of the experiment.

So, when the dry extract of the common oleander plant was added to the dry extract of kashqarbeda and administered to animals, the anticoagulant effect of kashqarbeda was significantly preserved. The hemostatic effect characteristic of the dry extract of the plant is reduced.

Conclusion: For the first time, the effect of a new drug consisting of a collection of common sedum and kashqarbeda plants and their dry extracts on the blood coagulation process was studied. As a result, a scientific basis was created for the enrichment of the medical field with a new drug that slows down the local blood clotting process with high efficiency, no side effects, and low cost.

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